DATA REPORT THYROID CANCER IN MASSACHUSETTS

The Massachusetts Cancer Registry, Massachusetts Department of Public Health May, 2007

PURPOSE & SUMMARY

This report provides descriptive and analytic information on the incidence of thyroid cancer in Massachusetts residents, using data from the Massachusetts Cancer Registry (MCR). Thyroid cancer rates have been increasing since 1984, with significant increases since 1997. The papillary form of thyroid cancer has accounted for 95% of this increase, with papillary tumors less than 2 centimeters accounting for 71% of the papillary increase. These changes mirror changes in the US and point to better tumor detection as an explanation of the increase. This report also briefly examines thyroid cancer mortality rates using data from the Massachusetts Registry of Vital Records and Statistics. Thyroid cancer has among the lowest mortality rates of all cancers.

SOURCES OF INCIDENCE & MORTALITY DATA

The Massachusetts Cancer Registry (MCR):

All Massachusetts incidence data are provided by the Massachusetts Cancer Registry, which is part of the Massachusetts Department of Public Health (MDPH). The MCR is a population-based cancer registry that began collecting reports of newly-diagnosed cancer cases in 1982. In 2003, the MCR collected reports from all Massachusetts acute care hospitals, one medical practice association, and selected physician specialties, including 230 dermatology offices, and 2 dermatopathology labs. The MCR also identified cancers noted on death certificates that were not previously reported to the MCR. The North American Association of Central Cancer Registries (NAACCR) has estimated that MCR case ascertainment is over 95% complete. The Massachusetts cancer cases presented in this report are primary cases of invasive thyroid cancer that were diagnosed among Massachusetts residents, unless noted otherwise. A primary case of thyroid cancer means that the cancer originated in the thyroid gland.

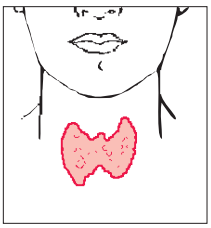
Surveillance, Epidemiology and End Results (SEER):

National data on cancer incidence are from the National Cancer Institute's SEER Program, an authoritative source on cancer incidence in the United States that collects and publishes data from registries in selected areas. The national cancer incidence data in this report include malignant cases from the 12 SEER areas (including Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, Utah, Los Angeles, San Jose-Monterey and Alaska). SEER rates are presented per 100,000 persons and are age-adjusted to the 2000 United States standard population.

Massachusetts Registry of Vital Records and Statistics:

Massachusetts death data were obtained from the MDPH's Registry of Vital Records and Statistics, which has legal responsibility for collecting reports of deaths of Massachusetts residents. The national mortality data are from the National Center for Health Statistics and include the entire United States.

THE EPIDEMIOLOGY OF THYROID CANCER



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The Thyroid Gland and Thyroid Cancer[1]:

The thyroid gland is located in the middle of the neck below the larynx (voice box) and just above the clavicles (collarbones). It is shaped like a bow tie, having two halves (lobes) joined by an isthmus. It is an endocrine gland, whose follicular cells make thyroid hormones to regulate physiological functions in the body such as heart rate, body temperature, and energy level. Its parafollicular, or C, cells make calcitonin, a regulator of the body's calcium metabolism.

There are four main types of thyroid cancer:

Papillary cancer of the thyroid is the most common, accounting for 70% of thyroid cancers. The peak onset age is between 30 and 50, with a female to male ratio of 3:1. The overall cure rate is very high, nearly 100% for small lesions in young patients.

Follicular cancer of the thyroid is the next most common type, accounting for about 15% of thyroid cancers. The peak onset age is between 40 and 60, with a female to male ratio of 3:1. The overall cure rate is also very high, nearly 95% for small lesions in young patients.

Medullary cancer of the thyroid accounts for about 5-8% of thyroid cancers. Unlike papillary and follicular thyroid cancers, which arise from thyroid hormone cells, medullary thyroid cancer arises from the parafollicular cells of the thyroid. About 20% of medullary thyroid cancer cases are the result of inheriting an abnormal gene. The overall ten-year survival rates are 90% for local disease, 70% for regional spread, and 20% for distant spread (See Technical Notes for a description of cancer stages). This cancer is more common in females than males, except for inherited cancers.

Anaplastic cancers of the thyroid are the least common (0.5-1.5%) and most deadly of all thyroid cancers and are most common in males (2:1) and after age 65. This cancer begins in the follicular cells and tends to grow and metastasize (spread) very quickly.[2] 50% of people have cancers which have spread to the lung at the time of diagnosis. Survival time is usually less than a year. Most of these cancers are so aggressively attached to vital neck structures that they are inoperable at the time of diagnosis.

Risk Factors for Thyroid Cancer:

Radiation – The thyroid gland can be affected by exposure to ionizing radiation. The thyroid glands of children are especially sensitive to radiation, much more so than the thyroid glands of adults.[3] During the 1940s and 1950s, children were sometimes treated with radiation for acne, fungal infections of the scalp, an enlarged thymus gland, or to shrink tonsils or adenoids. Various studies have linked these treatments to an increased risk of thyroid cancer.[4] In addition to exposure to ionizing radiation for medical treatment, exposure to nuclear fallout has been linked to increased thyroid cancer in both Chernobyl and Hiroshima/Nagasaki. The level of fallout from above-ground nuclear testing in the western United States during the 1950s was much lower than in Chernobyl or Hiroshima/Nagasaki, and a link between nuclear fallout and thyroid cancer has not been proven in this population.[4]

Genetics – As mentioned in the previous section, about 20% of medullary thyroid cancers result from inheriting an abnormal gene. These cases are known as familial medullary thyroid carcinoma (FMTC). People with certain inherited medical conditions such as Gardner syndrome and familial polyposis are also at a higher risk for thyroid cancer. Certain other families have been found to have an excess number of papillary thyroid cancers, but the genetic basis for this is not known.[4]

Sex – For reasons which are not clear, benign thyroid nodules and thyroid cancers occur almost three times more often in females than in males.

Other – Other studies have explored the associations of thyroid cancer with oral contraceptive use, age at menarche, parity (number of pregnancies), and diet.[5,6,7] There are as yet no consistent findings among these studies.

With the exception of most of the familial cases of medullary thyroid cancer which can be treated early or prevented due to genetic blood tests now available, most people with thyroid cancer have no known risk factors and it is not possible to reliably prevent most cases of this disease.[4] Furthermore, incidence rates in Massachusetts have continued to increase in people born after nuclear testing and routine childhood irradiation ceased.

Thyroid Cancer Incidence Trends:

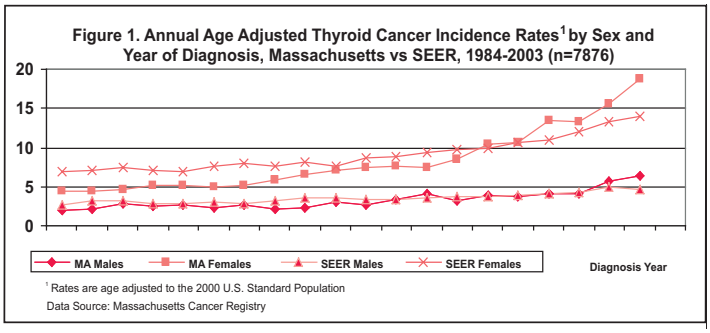
From 1999-2003 in Massachusetts, there were 2531 cases of thyroid cancer among females, with a rate of 14.3 per 100,000, making it the eighth most common cancer among females. This rate was much lower than that of breast cancer (141.3 per 100,000), lung cancer (62.0 per 100,000) and colorectal cancer (50.9 per 100,000). There were 811 cases of thyroid cancer among males, with a rate of 4.8 per 100,000, making it the eighteenth most common cancer among males. This was much lower than prostate cancer (185.1 per 100,000), lung cancer (89.1 per 100,000) and colorectal cancer (72.2 per 100,000). Despite the lower ranking of thyroid cancer among both sexes, incidence rates increased by 81% for females and 66% for males between 1999 and 2003 – the greatest rate increases among all cancers for both males and females during this period.

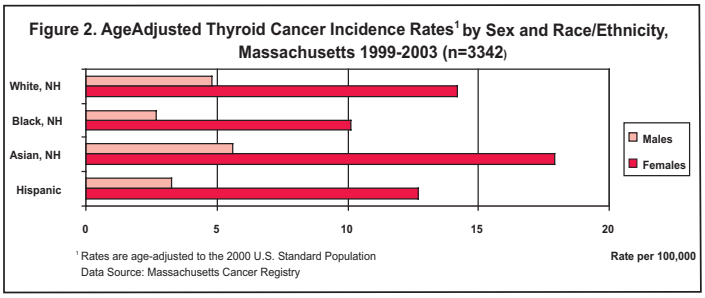
The dramatic increase of thyroid cancer in Massachusetts is reflected in other studies in the United States[8,9,10], Australia[11], France[12], and Luxembourg[13]. These reports all point to the papillary form of thyroid cancer as driving the increases, and nearly all point to better

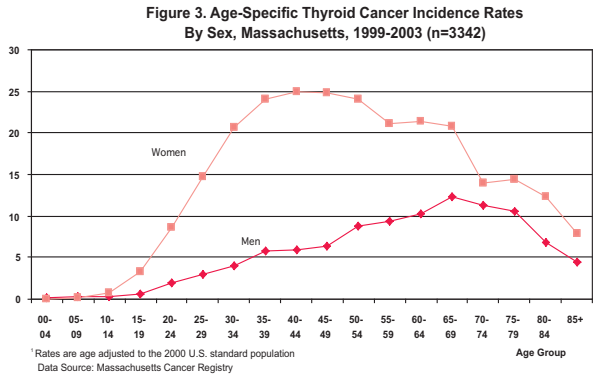
detection of smaller tumors as a cause for the increase. Additionally, the most recent Annual Report to the Nation on the Status of Cancer (1975-2003) reported that thyroid cancer incidence rates among females have increased since 1981, with the rate of this increase doubling in 1993 and again in 2000.[14] The annual Massachusetts and SEER age-adjusted rates for thyroid cancer were calculated for the years 1984-2003 (Figure 1). The increase in rates among Massachusetts females are the most dramatic, surpassing the increase nationally. The rates for males in Massachusetts remained relatively stable, with a small increase after 2001.

Thyroid Cancer Incidence by Race/Ethnicity:

Among the four major race/ethnicity groups from 1999-2003, the female to male ratio was 3:1 for all groups. Asian, non-Hispanic cases had the highest rates overall (Figure 2). Two studies in San Francisco that focused on elevated rates of thyroid cancer among Southeast Asian females pointed to a greater prevalence of goiter and thyroid nodules among this population as accounting for the higher incidence rates. Additionally, females born in the Philippines and Vietnam had higher rates than females of Filipino and Vietnamese ethnicity born in the United States.[15,16] The number of cases for specific Asian ethnicities in Massachusetts (Japanese, Indian, Vietnamese, etc.) were too small for further analysis.







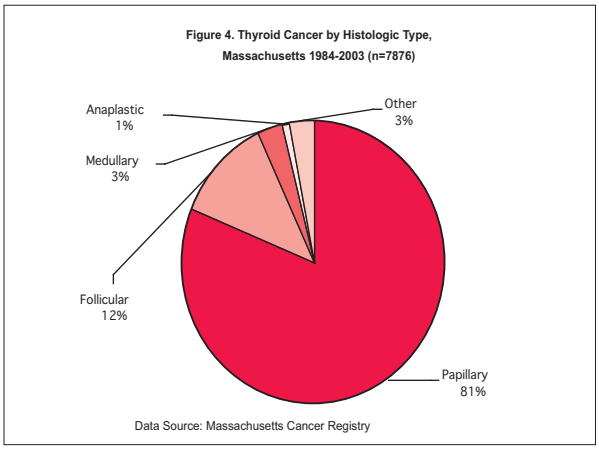
Thyroid Cancer Incidence by Age:

From 1999-2003, the peak age at diagnosis for thyroid cancer was 40 to 45 for females and 65 to 69 for males. For every adult age group, the rates among females were higher than those among males, nearly five times higher among 40-45-year-olds. (Figure 3)

Thyroid Cancer Incidence by Histological Type:

From 1984-2003, papillary cancer represented 81% of all thyroid cancers diagnosed, followed by follicular cancer (12%), medullary cancer (3%) and anaplastic cancer (1%). (Figure 4) An analysis of age-adjusted rates for the four major types of thyroid cancer from 1984 to 2003 revealed a three-fold increase in the papillary form of thyroid cancer, which will be explored in greater detail. (Figure 5)

When comparing the number of new cases of thyroid cancer in 1984 with those in 2003, papillary cancer accounted for 95% of the increase. A Joinpoint analysis of trends in papillary thyroid cases indicated a significant increase after 1997, with an annual percent change of 14.3% from 1998 to 2003. The other forms of thyroid cancer have experienced stable, non-significant changes in rates during this time period. Since papillary cases of thyroid cancer appear to be driving the trend, this report will now focus on that type of thyroid cancer.



Early Detection and the Significant Increase in Papillary Thyroid Cancer:

The increases in the papillary form of thyroid cancer in Massachusetts are similar to the trends in other parts of the country and the world. A recent study in the *Journal of the American Medical Association (JAMA)* linked the increasing incidence to better detection of papillary thyroid microcarcinomas (PTMC), tumors less than 1 centimeter in diameter.[8] The introduction of fine needle aspiration biopsy and ultrasound imaging during the 1980s has aided in the earlier detections of these small tumors.[8] Support for earlier detection as the major reason for the increase of papillary cases can be found in autopsy studies in which the papillary form of thyroid cancer was a common finding despite its never having caused symptoms during a person's life.[17,18]

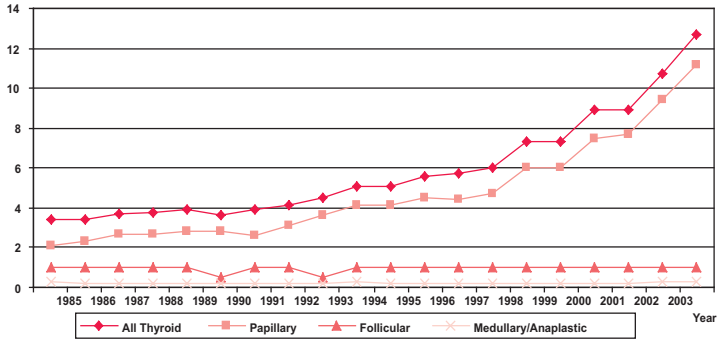
Trends in Papillary Thyroid Tumor Size:

Since the MCR began to collect data on tumor size in 1995, data on tumor sizes of papillary thyroid cancers are limited to the period of 1995 to 2003. The size categories (0-1 cm, 1.1-2 cm, 2.1-5 cm and larger than 5 cm) were based on categories defined in the *JAMA* article on the increasing incidence of thyroid cancer in the United States from 1973 to 2002.[8] All tumor size groups 5 cm or smaller experienced increases from 1995 to 2003. Joinpoint analyses revealed significant annual percent change increases for the 0-1 cm group (15.8%), the 1.1-2 cm group (13.1%) and the 2.1-5 cm group (12.3%). The relative contributions to the increase in papillary tumors by size are as follows: those 1 cm or less (PTMCs) accounted for 41% of the increase, those 1.1 to 2 cm accounted for 30%, and those 2.1 to 5 cm accounted for 26%. There was no significant change among the largest tumor sizes (Figure 6).

These data reveal that tumors are being diagnosed at smaller sizes, especially the PTMCs. According to a recent study in the *Journal of Clinical Endocrinology*, thyroid carcinomas less than 1 cm are almost always PTMCs, and are generally diagnosed after fine needle aspiration biopsy or incidentally during thyroid surgery for benign thyroid disorders.[19]

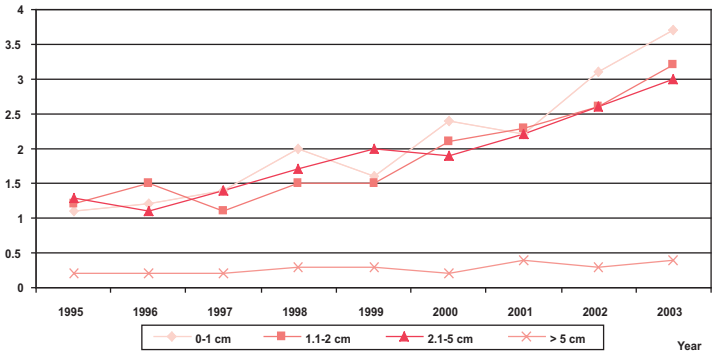
When comparing the four tumor size groups for all types of thyroid cancer, the proportion of papillary thyroid cases significantly decreased as the size of the tumor increased. For the two smallest groups, there were no anaplastic cases. This finding supports the fact that anaplastic tumors are faster growing and are detected at larger sizes. It should be noted that during this time period, data on tumor size were missing for 11% of all thyroid cancer cases, with disproportionately higher amounts of missing data for the following: anaplastic cases, blacks, Hispanics and females. (Figure 7)

Figure 5. Age-Adjusted Incidence Rates[1] of Thyroid Cancer by Histologic Type, Massachusetts, 1984-2003 (n=7876)



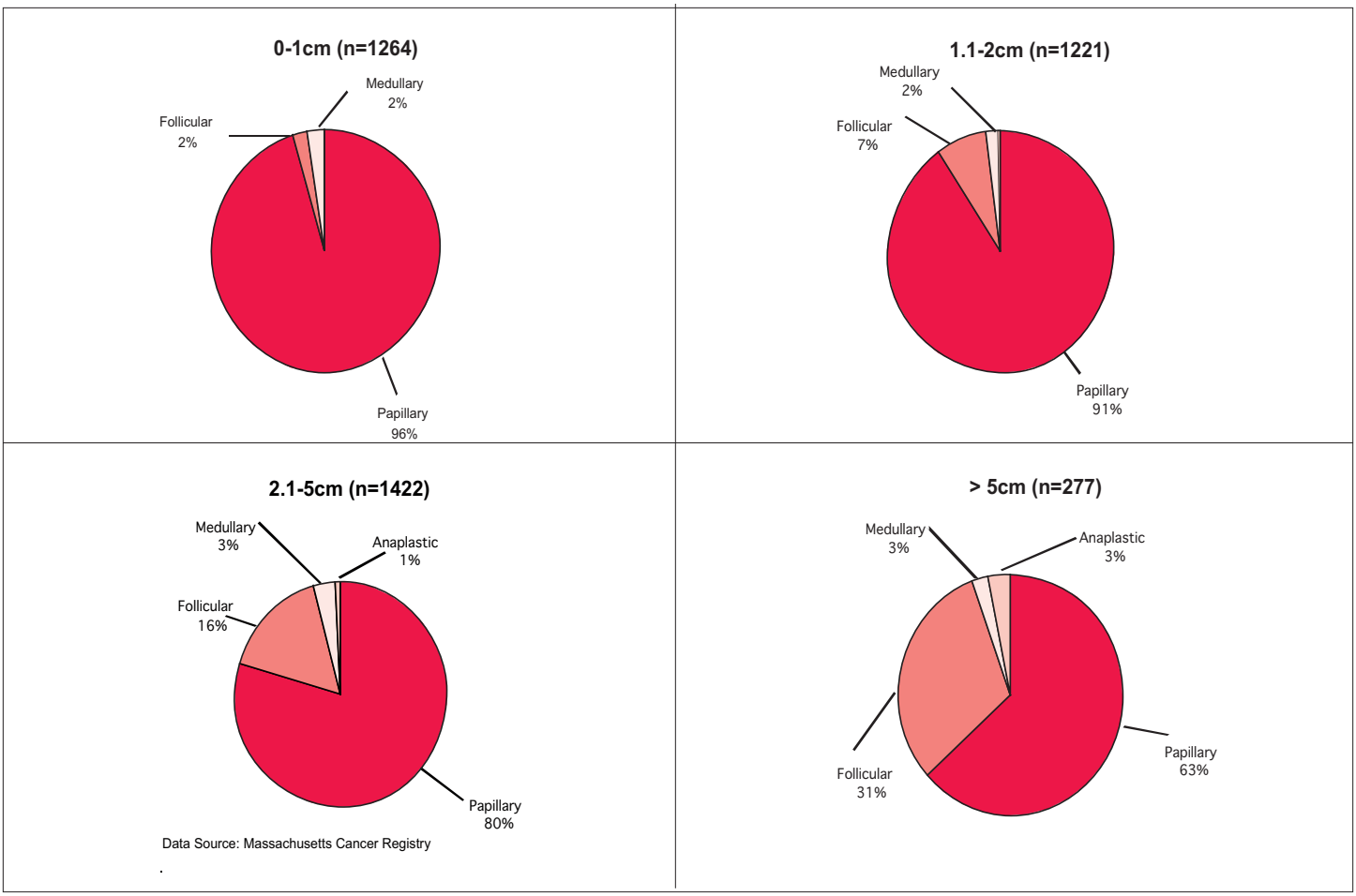
[1] Rates are age adjusted to the 2000 U.S. population
Data Source: Massachusetts Cancer Registry

Figure 6: Age Adjusted Trends[1] in Tumor Size of Papillary Thyroid Cancers, Massachusetts, 1995-2003 (n=4184)



[1] Rates are age adjusted to the 2000 U.S. standard population
Date Source: Massachusetts Cancer Registry

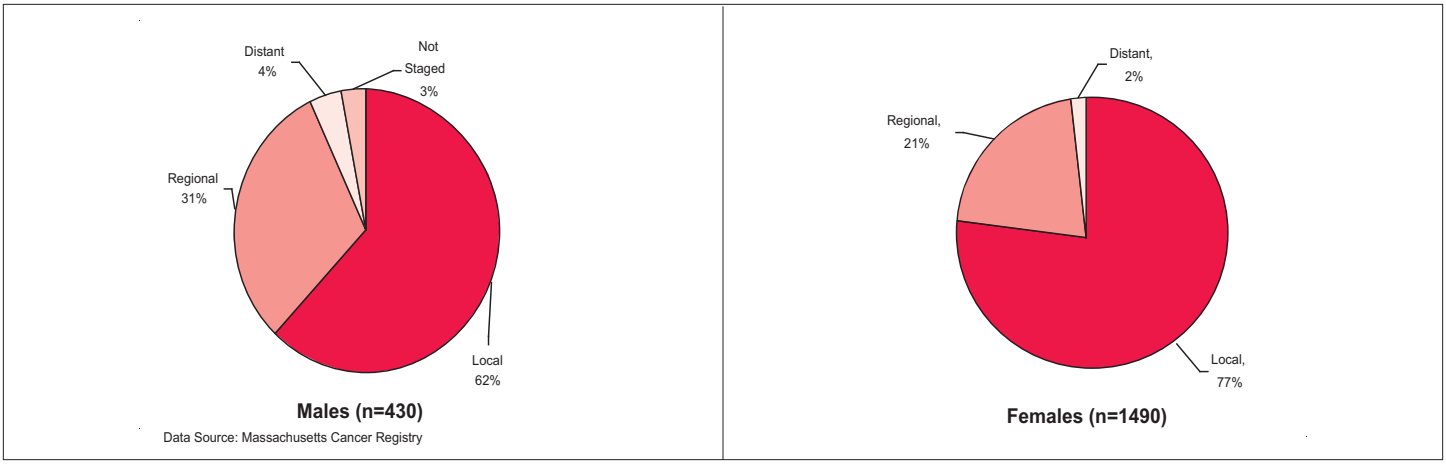
Figure 7. Tumor Size Variation by Type of Thyroid Cancer, Massachusetts 1995-2003



Thyroid Cancer Incidence by Sex:

As shown earlier in this report, the female to male ratio for thyroid cancer is approximately 3:1 in Massachusetts. From 1995 to 2003, the median tumor size for papillary thyroid cancer was smaller for females than for males. The mean tumor sizes at diagnosis dropped significantly from 2.5 cm in 1995 to 1.7 cm in 2003 for females, and non-significantly from 2.6 cm to 2.1 cm for males. In addition to tumor sizes being smaller, the stage at diagnosis was also more likely to be local for females (77%) than for males (62%). Males were more likely to be diagnosed at a regional stage (31%) compared to females (21%). There was no significant difference between the sexes for distant stage diagnoses. Due to changes in the staging criteria in 2000, the data presented are for 2001 to 2003. (Figure 9)

Figure 8. Stage at Diagnosis of Thyroid Cancer by Sex, Massachusetts, 2001-2003



Thyroid Cancer Mortality:

Mortality from thyroid cancer is very low, with the exception of the rare anaplastic form of the disease. From 1999-2003, the mortality rates for males and females were 0.4/100,000 and 0.5/100,000 respectively, making this one of the cancers with the lowest mortality rates. Since the Vital Statistics data do not differentiate among the four types of thyroid cancer, it was not possible to ascertain the mortality rates for anaplastic cancers as opposed to the other types of thyroid cancer. National mortality rates were similar to the rates in Massachusetts.[14]

DATA SUMMARY

- Thyroid cancer incidence rates for males and females combined in Massachusetts increased significantly between 1984 and 2003, from 3.4/100,000 in 1984 to 12.7/100,000 in 2003.
- From 1995 to 2003, incidence rates among males increased by 66%, from 3.8 to 6.3/100,000. Rates among females increased by 81%, from 10.7 to 18.7/100,000. The ratio of female to male cases was 3:1 during this period. This is consistent among the four major racial/ethnic groups.
- From 1999-2003, thyroid cancer incidence rates were elevated for Asians in Massachusetts, which mirrors trends in other parts of the United States. The numbers for specific Asian ethnicities in Massachusetts were too small for a meaningful analysis.
- From 1984 to 2003, 95% of the increase in thyroid cancer has been attributable to increases in the papillary form of the cancer.
- The incidence rate of papillary thyroid cancer has increased significantly since 1997, with an annual percentage increase of 14.3%.
- Among papillary thyroid cancer cases from 1995 to 2003, tumors less than 5 cm increased significantly compared to those larger than 5 cm. The tumors 1 cm or less, the papillary thyroid microcarcinomas, accounted for 41% of the increase, those 1.1-2.0 cm accounted for 30%, and those 2.1 to 5.0 cm accounted for 26%.
- The mean size of papillary tumors has been larger for males compared with females for the years 1995 to 2003. During this period, the mean tumor sizes at diagnosis dropped from 2.5 cm to 1.7 cm for females, and 2.6 cm to 2.1 cm for males
- From 2001 to 2003, females were significantly more likely to be diagnosed at the local stage than males. Males were significantly more likely to be diagnosed at the regional stage than females, and both sexes were equally likely to be diagnosed at the distant stage.
- From 1999-2003, mortality rates were approximately 0.5/100,000 for both sexes, a rate comparable to the national rate.

CONCLUSIONS & LIMITATIONS

- The reason for the increases in thyroid cancer tumors 1 cm and less appear to be the result of better detection with fine needle aspiration biopsy and ultrasound. The increase in the larger tumors between 1.1 and 5 cm suggests better clinician awareness of thyroid cancer as well as an increase in neck palpations as part of a routine medical examination.
- The greater increase of papillary cases in females, the larger mean size of tumors in males, and the later stage at diagnosis in males from 2001 to 2003 indicate detection among females who may be utilizing the health care system more than males.
- As the MCR registry is a surveillance database, there is no information on radiation exposure, diet or hormonal factors that could be related to thyroid cancer cases.

TECHNICAL NOTES AND DEFINITIONS

Age-adjusted rate – a rate that takes into account the age structure of an area, allowing for the comparison of areas with different age distributions. Age-adjusted rates were calculated by weighting the age-specific rates of a given year by the age distribution of the 2000 U.S. standard population. The weighted age-specific rates were then added to produce the adjusted rate for all ages combined. Rates should only be compared if they have been adjusted to the same standard population.

Age-specific rate – a rate among people of a particular age range in a given time period. Age-specific rates were calculated by dividing the number of people in an age group who were newly diagnosed with cancer (incidence) or died of cancer (mortality) by the number of people in that same age group overall.

Incidence – the number of people who are newly diagnosed with a disease, condition, or illness during a particular time period. The incidence data presented here were coded using the third edition of the International Classification of Disease for Oncology (ICD-O-3) coding system. Thyroid cancer cases were defined with an ICD-O-3 code of C73.9; histologies 9590-9989 were excluded. All cancers were invasive. The following histologies were used to define the four main types of thyroid cancer:

Papillary – 8050, 8051, 8052, 8130, 8260, 8340, 8341, 8342, 8343, 8344, 8350, 8540.
Follicular – 8290, 8330, 8331, 8332, 8335.
Medullary – 8345, 8346, 8347, 8510.
Anaplastic – 8020, 8021, 8032.

Mortality – the number of people who died of a disease, condition, or illness during a particular time period. The mortality data presented here were coded using the tenth edition of the International Classification of Diseases (ICD-10). Thyroid cancer was defined as C73 (ICD-10).

Population estimates – rates were calculated using population estimates obtained from the Massachusetts Department of Public Health (MDPH) using the Massachusetts Community Health Information Profile (MassCHIP) demographic/census files.

Race/ethnicity – The categories presented in this report are mutually exclusive. Cases are only included in one race/ethnicity category. The race/ethnicity tables include the categories white, non-Hispanic; black, non-Hispanic; Asian, non-Hispanic; and Hispanic.

Stages of Cancer – For this report, there were three stages of cancer utilized: localized cancer was found only in the body part (organ) where it began and has not spread; regional cancer has spread beyond the original point of origin to the nearest surrounding parts of the body (other tissues); and distant cancer has spread to parts of the body far away from the original point where it began.

Trend – Trend data were analyzed using the Joinpoint Regression Program from the National Cancer Institute. This program identifies joined line segments that are connected by points where the trend changes. An annual percent change (APC) describes the average change per year over the line segment. A positive APC corresponds to an increasing trend, and a negative APC corresponds to a decreasing trend. Joinpoint analysis determines whether or not the APC is significant.

Significant differences between proportions in this report had p values less than 0.05.

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